

### III. Rejections Under 35 U.S.C. §112, First Paragraph

Claim 18 was rejected under 35 U.S.C. §112, first paragraph, as not being enabled. The Examiner argued that the specification did not contain guidance sufficient to allow one skilled in the art to make oligonucleotide probes containing a phosphoramidate linkage (N3'-->P5') between the terminal and penultimate nucleotides. However, the applicant submits that such methodology was well known in the art at the time of the present invention, and therefore need not be repeated in the specification.

In support of this position, enclosed herewith are copies of three illustrative references showing that the requisite synthetic methodology was well known.

Gryaznov et al., Nucl. Acids Res. 20:3403 (1992), discloses synthesis of oligonucleotides having internal bridging phosphoramidates by way of dimer blocks (I) and/or (X) shown in the first column of page 3406. U.S. Patent No. 5,476,925 (of record) is based on this disclosure.

Gryaznov and Chen, JACS 116:3143 (1994), discloses a method of synthesizing oligos with any number of internal N3'-->P5' phosphoramidate linkages.

Bannwarth, Helv. Chim. Acta 71:1517 (1988), discloses synthesis of oligos having internal N5'-->P3' phosphoramidate linkages.

"A patent need not teach, and preferably omits, what is well known in art." Hybritech Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 231 USPQ 81 (CAFC 1986). Given that methods for synthesizing oligonucleotides containing such phosphoramidate linkages were well known in the art, the specification meets the enablement requirement. Withdrawal of the rejection is therefore respectfully requested.

### IV. Rejections Under 35 U.S.C. §112, Second Paragraph

Claims 18 and 19 were rejected under 35 U.S.C., second paragraph, as being indefinite (i) due to the Examiner's uncertainty regarding the ranges of j and k (claims 18 and 19), (ii) because the symbols j and k were inadvertently used in claim 19 instead of

s and w, and (iii) because of the phrase "labeled chain terminating moiety" (claims 18 and 19).

With regard to the ranges of j and k in claim 18, and s and w in claim 19, the applicant submits that the recited ranges are not in conflict. In particular, there is nothing in the specification to require that the range for k cannot be from 0 to 12 as recited, rather than 0 to 11 as suggested by the examiner. Nor is this in conflict with the limitation that the sum of  $j + k$  is less than or equal to 12. For example, if j is 0, k is 12 or less. If k is 0, j is 12 or less. Similar reasoning applies to s and w in claim 19. A person of ordinary skill in the art would have no difficulty understanding the metes and bounds of the recited ranges.

With regard to antecedent basis for k and j in claim 19, this claim has been amended to correct an inadvertent typographical error, in accordance with the Examiner's suggestion.

Finally, the phrase "labeled chain terminating moiety" has been amended in claims 18 and 19 to --labeled, non-extendable chain terminating moiety-- to recite that the moiety is not extendable by DNA polymerase.

V. Rejection Under 35 U.S.C. §102(b)/103(a)

Claim 19 was rejected under either 35 U.S.C. §102(b) or 103(a) as being unpatentable over Duck et al. (U.S. Patent No. 5,011,769). This rejection is believed moot in light of the amendment to claim 19.

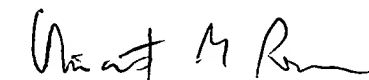
VI. Conclusion

In view of the foregoing, the applicant submits that the claims pending in the application are in condition for allowance. A Notice of Allowance is therefore respectfully requested.

Date: \_\_\_\_\_

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Respectfully submitted,



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